



2-20-07

1626

Attorney's Docket No.: 20750-038US1 / 029.US2.PCT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Graeme Semple, et al. Art Unit : 1626
Serial No. : 10/530,902 Examiner : Rebecca L. Anderson
Filed : April 8, 2005 Conf. No. : 2895
Title : 5-SUBSTITUTED 2H-PYRAZONE-3-CARBOXYLIC ACID DERIVATIVES AS
ANTILIPOLYTIC AGENTS FOR THE TREATMENT OF METABOLIC-
RELATED DISORDERS SUCH AS DYSLIPIDEMIA

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INFORMATION DISCLOSURE STATEMENT

Applicants request consideration of the references listed on the attached PTO-1449 form. Under 37 C.F.R. § 1.98 (a)(2)(ii), only copies of foreign patent documents and/or non-patent literature are enclosed. Copies of any listed U.S. patents or U.S. patent application publications can be provided upon request. A copy of a communication from a foreign patent office in a counterpart application is also enclosed.

This statement is being filed within three months of the filing date of the application or before the receipt of a first Office Action on the merits. Please apply any charges or credits to Deposit Account No. 06-1050.

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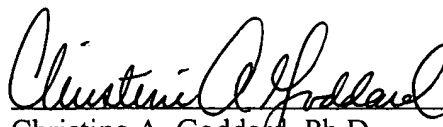
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Applicant : Graeme Semple, et al.
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Page : 2 of 2

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Respectfully submitted,

Date: February 15, 2007


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PTO/SB/08a (08-03)

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**INFORMATION DISCLOSURE
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Sheet 1 of 6

Complete if Known

| | |
|------------------------|---------------------|
| Application Number | 10/530,902 |
| Filing Date | April 8, 2005 |
| First Named Inventor | Graeme Semple |
| Art Unit | 1626 |
| Examiner Name | Anderson, Rebecca L |
| Attorney Docket Number | 29.US2.PCT |

U.S. PATENT DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Document Number | Publication/Issue Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
|------------------------|--------------------------|--|--------------------------------------|--|---|
| | | Number - Kind Code ² (if known) | | | |
| | FL | US-2005/154024 | 07-14-2005 | Bryans <i>et al.</i> , | |
| | FM | US-2005/182108 | 08-18-2005 | Carson <i>et al.</i> , | |
| | FN | US-6,444,816 B1 | 09-03-2002 | Das <i>et al.</i> , | |

FOREIGN PATENT DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Foreign Patent Document | Publication Date/Filing Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
|------------------------|--------------------------|---|---|--|--|----------------|
| | | Country Code ³ - Number ⁴ - Kind Code ⁵ (if known) | | | | |
| | FO | WO2003/032928 A1 | 04-22-2004 | Arena Pharmaceuticals, Inc. | | |
| | FP | WO2004/054974 | 07-01-2004 | SmithKline Beecham Corporation | | |
| | FQ | WO2005/009965 | 02-03-2005 | Pfizer Ltd. | | |
| | FR | WO2005/084663 | 09-15-2005 | Janssen Pharmaceutica | | |
| | FS | WO2006/023750 | 03-02-2006 | Merck & Co., Inc. | | |
| | FT | WO2006/032519 | 03-30-2006 | Hoffmann-La Roche | | |
| | FU | WO2006/032851 | 03-30-2006 | Bioliopx AB | | |
| | FV | WO2006/032852 | 03-30-2006 | Bioliopx AB | | |
| | FW | WO2006/052569 | 05-18-2006 | Arena Pharmaceuticals, Inc. | | |
| | FX | WO02/22601 | 03-21-2002 | Vertex Pharmaceuticals, Inc. | | |
| | FY | WO00/69849 | 11-23-2000 | Ortho-McNeil Pharmaceutical, Inc. | | |
| | FZ | WO03/099793 | 12-04-2003 | Takeda Chemical Industries, Ltd. | | |
| | GA | WO2004/033431 | 04-22-2004 | Arena Pharmaceuticals, Inc. | | |
| | GB | GB 1048104 | 11-09-1966 | The Upjohn Company | | |
| | GC | JP 54014968 | 02-03-1979 | Taiho Pharmaceutical Co. Ltd. | | |
| | GD | HU184940B | 11-28-1984 | Gyogyszerkutato Intezet | | |

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Sheet 2 of 6

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| Filing Date | April 8, 2005 |
| First Named Inventor | Graeme Semple |
| Art Unit | 1626 |
| Examiner Name | Anderson, Rebecca L |
| Attorney Docket Number | 29.US2.PCT |

NON PATENT LITERATURE DOCUMENTS

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|------------------------|--------------------------|---|----------------|
| | GE | FROESCH <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid on adipose tissue. I. Inhibition of lipolysis, effects on glucose, fructose, and glycogen metabolism in vitro and comparison with insulin. <i>Molecular Pharmacol.</i> (1967), 3(5), 429-41 | |
| | GF | MUGNAINI <i>et al.</i> Heterocyclic syntheses with propargyl alcohol and butynediol. II. <i>Classe sci. fis., mat. e nat.</i> (1953), 14, 275-80 | |
| | GG | MUGNAINI <i>et al.</i> Heterocyclic syntheses with propargyl alcohol and butynediol. <i>Classe sci. fis., mat. e nat.</i> (1953), 14, 95-8 | |
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| | GI | PANIZZI <i>et al.</i> Heterocyclic syntheses. VII. Some pyrazolic ketones. <i>Gazzetta Chimica Italiana</i> (1946), 76, 66-77 | |
| | GJ | MELANI <i>et al.</i> Synthesis of 5H-10,11-dihydropyrazolo[5,1-c][1,4]benzodiazepine derivatives. II. <i>Journal of Heterocyclic Chemistry</i> (1984), 21(3), 813-15 | |
| | GK | KLAGES <i>et al.</i> Pyrazoles from 1:3-diketones and alkyl diazoacetates. <i>Journal fuer Praktische Chemie</i> (1902), 65(ii), 387-93 | |
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| | GN | International Search Report, WO 2005/011677, 12/10/2004 | |
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| | GP | TAVINTHARAN <i>et al.</i> The benefits of niacin in atherosclerosis. <i>Current atherosclerosis reports</i> (2001), 3(1), 74-82 | |
| | GQ | CARLSON <i>et al.</i> Nicotinic acid: the broad-spectrum lipid drug. A 50th anniversary review. <i>Journal of Internal Medicine</i> (2005), 258(2), 94-114 | |

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| Examiner Signature | | Date Considered | |
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Sheet 3 of 6

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| Application Number | 10/530,902 |
| Filing Date | April 8, 2005 |
| First Named Inventor | Graeme Semple |
| Art Unit | 1626 |
| Examiner Name | Anderson, Rebecca L |
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NON PATENT LITERATURE DOCUMENTS

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|---------------------|-----------------------|---|----------------|
| | GR | LORENZEN <i>et al.</i> Characterization of a G protein-coupled receptor for nicotinic acid. <i>Molecular Pharmacology</i> (2001), 59(2), 349-357 | |
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| | GT | TUNARU <i>et al.</i> PUMA-G and HM74 are receptors for nicotinic acid and mediate its anti-lipolytic effect. <i>Nature Medicine</i> (2003), 9(3), 352-355 | |
| | GU | ZHANG <i>et al.</i> , Niacin mediates lipolysis in adipose tissue through its G-protein coupled receptor HM74A. <i>Biochemical and Biophysical Research Communications</i> (2005), 334(2), 729-732 | |
| | GV | BENYO <i>et al.</i> GPR109A (PUMA-G/HM74A) mediates nicotinic acid-induced flushing. <i>Journal of Clinical Investigation</i> (2005), 115(12), 3634-3640 | |
| | GW | O'KANE <i>et al.</i> A comparison of acipimox and nicotinic acid in type 2b hyperlipidaemia. <i>British journal of clinical pharmacology</i> (1992), 33(4), 451-3 | |
| | GX | JIRKOVSKY <i>et al.</i> , Hypolipidemic 4,5-dihydro-4-oxo-5,5-disubstituted-2-furancarboxylic acids. <i>Journal of Medicinal Chemistry</i> (1982), 25(10), 1154-6 | |
| | GY | HUNNINGHAKE <i>et al.</i> Controlled trial of acifran in type II hyperlipoproteinemia. <i>Clinical pharmacology and therapeutics</i> (1985), 38(3), 313-7 | |
| | GZ | SEKI <i>et al.</i> , Studies on hypolipidemic agents. II. Synthesis and pharmacological properties of alkylpyrazole derivatives. <i>Chemical & Pharmaceutical Bulletin</i> (1984), 32(4), 1568-77 | |
| | HA | VAN HERK <i>et al.</i> , Pyrazole Derivatives as Partial Agonists for the Nicotinic Acid Receptor. <i>Journal of Medicinal Chemistry</i> (2003), 46(18), 3945-3951 | |
| | HB | MAHBOUBI <i>et al.</i> , Triglyceride modulation by acifran analogs: activity towards the niacin high and low affinity G protein-coupled receptors HM74A and HM74. <i>Biochemical and Biophysical Research Communications</i> (2006), 340(2), 482-490 | |
| | HC | FROESCH <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid on adipose tissue. II. Antilipolytic and hypoglycemic effects in vivo. <i>Molecular Pharmacol.</i> (1967), 3(5), 442-52 | |
| | HD | Beilstein Records (BRN): 10958, Chemical Name (CN): 4-methyl-5-propionyl-1(2) <i>H</i> -pyrazole-3-carboxylic acid | |
| | HE | Beilstein Records (BRN): 14055, Chemical Name (CN): 4-methyl-5-propionyl-1(2) <i>H</i> -pyrazole-3-carboxylic acid ethyl ester | |

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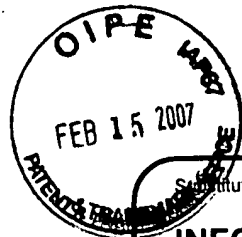
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Sheet 4 of 6

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|---------------------|-----------------------|---|----------------|
| | HF | GERRITSEN <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic acid, U-19425, on FFA [free fatty acid] mobilization. <i>Advan. Exp. Med. Biol.</i> (1969), 4 93-103 | |
| | HG | BIZZI <i>et al.</i> , Correlation between the effect of drugs on plasma free fatty acids and on tissue triglycerides. <i>Advan. Exp. Med. Biol.</i> (1969), 4 201-11 | |
| | HH | GUNDERSEN <i>et al.</i> , Effects of 5-methylpyrazole-3-carboxylic and (U-19,425) and nicotinic acid (NA) on free fatty acids (FFA), triglycerides (TG), and cholesterol in man. <i>Advan. Exp. Med. Biol.</i> (1969), 4, 213-26 | |
| | HI | KIENER, Enzymic oxidation of methyl groups in heteroarenes: a versatile method for the preparation of heteroaromatic carboxylic acids. <i>Angew. Chem., Int. Ed. Engl.</i> , 1992, 31(6), 774-5 | |
| | HJ | AKTORIES <i>et al.</i> , Inhibition of adenylate cyclase and stimulation of a high affinity GTPase by the antilipolytic agents, nicotinic acid, acipimox and various related compounds. <i>Arzneimittel-Forschung</i> (1983), 33(11), 1525-7 | |
| | HK | PRYOR <i>et al.</i> , Purification of maize alcohol dehydrogenase and competitive inhibition by pyrazoles. <i>Biochemistry International</i> (1982), 4(4), 431-8 | |
| | HL | BIZZI <i>et al.</i> , Effects of antilipolytic agents on glucose utilization by adipose tissue. <i>Biochemical Pharmacology</i> (1973), 22(6), 763-8 | |
| | HM | MYLES <i>et al.</i> , The development of tolerance to antilipolytic agents in rats. <i>Biochemical Pharmacology</i> (1985), 34(2), 269-74 | |
| | HN | STRATTON <i>et al.</i> , The development of tolerance to antilipolytic agents by isolated rat adipocytes. <i>Biochemical Pharmacology</i> (1985), 34(2), 275-9 | |
| | HO | COTTINEAU <i>et al.</i> , Synthesis and hypoglycemic evaluation of substituted pyrazole-4-carboxylic acids. <i>Bioorganic & Medicinal Chemistry Letters</i> (2002), 12(16), 2105-2108 | |
| | HP | HAMILTON <i>et al.</i> , The inhibition of mammalian D-amino acid oxidase by metabolites and drugs. Inferences concerning physiological function. <i>Bioorganic Chemistry</i> (1982), 11(3), 350-70 | |
| | HQ | ISSEKUTZ, Effect of nicotinic acid, 5-methylpyrazole-3-carboxylic acid (U-19425), and dibutylrly cyclic AMP on renal gluconeogenesis. <i>Canadian Journal of Physiology and Pharmacology</i> (1971), 49(2), 102-5 | |
| | HR | REIMLINGER <i>et al.</i> , Syntheses with silver or sodium pyrazoles. II. Reactions of the silver salts of methylpyrazoles with halogens. <i>Chemische Berichte</i> (1970), 103(6), 1949-53 | |
| | HS | SEKIHACHI <i>et al.</i> , Synthesis and chromophoric properties of symmetrical bis-heteroannulated diketopiperazines: diimidazo- and dipyrazolo-piperazinediones. <i>Dyes and Pigments</i> (1996), 32(1), 43-58 | |
| | HT | TIHANYI <i>et al.</i> , Pyrazolecarboxylic acid hydrazides as antiinflammatory agents. New selective lipoxygenase inhibitors. <i>European Journal of Medicinal Chemistry</i> (1984), 19(5), 433-9 | |

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|---------------------|-----------------------|---|----------------|
| | HU | BARALDI <i>et al.</i> , Synthesis, antibacterial activity and structure-activity relationships of N-substituted 4-diazopyrazole-5-carboxamides. 2. <i>Farmaco</i> (1991), 46(11), 1337-50 | |
| | HV | ALBERTI <i>et al.</i> , Alkylpyrazoles. <i>Farmaco, Edizione Scientifica</i> (1961), 16 527-39 | |
| | HW | ALEMAGNA <i>et al.</i> , Pyrazole synthesis from α -dicarbonyl compounds. <i>Gazzetta Chimica Italiana</i> (1963), 93(6), 748-56 | |
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| | HY | BERINGER <i>et al.</i> , Attempts towards oral diabetes therapy by means of inhibition of lipolysis with 5-methylpyrazole-3-carboxylic acid. <i>Hormone and Metabolic Research</i> (1970), 2(2), 81-5 | |
| | HZ | MISHRA <i>et al.</i> , A heteroaromatic acid from marine sponge <i>Suberites vestigium</i> . <i>Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry</i> (1998), 37B(2), 199-200 | |
| | IA | BANKS, Selectfluor reagent F-TEDA-BF ₄ in action: tamed fluorine at your service. <i>Journal of Fluorine Chemistry</i> (1998), 87(1), 1-17 | |
| | IB | MIETHCHEN <i>et al.</i> , Micelle-activated reactions. I. Micelle-activated iodination and partial dehalogenation of pyrazoles and 1,2,4-triazoles. <i>Journal fuer Praktische Chemie</i> (Leipzig) (1989), 331(5), 799-805 | |
| | IC | SAHA <i>et al.</i> , Mixed-ligand complexes of cobalt(II) and nickel(II) with 1-hydroxymethyl-5(3)-methylpyrazole-3(5)-carboxylic acid and heterocyclic amines. <i>Journal of the Indian Chemical Society</i> (1985), 62(2), 96-9 | |
| | ID | SAHA <i>et al.</i> , Synthesis, characterization and coordinating properties of a new benzimidazolylpyrazole: cobalt(II), nickel(II) and copper(II) complexes of 5-methyl-3-(2'-benzimidazolyl)pyrazole. <i>Journal of the Indian Chemical Society</i> (1993), 70(11-12), 1035-42 | |
| | IE | PARAMESWARAN <i>et al.</i> , Secondary metabolites from the sponge <i>Tedania anhelans</i> : isolation and characterization of two novel pyrazole acids and other metabolites. <i>Journal of Natural Products</i> (1997), 60(8), 802-803 | |
| | IF | MANAEV <i>et al.</i> , Dimethylpyrazole-based syntheses. V. Nitration of 4-halopyrazole-3- and 5-carboxylic acids. <i>Zhurnal Obshchei Khimii</i> (1982), 52(11), 2592-8 | |
| | IG | AKTORIES <i>et al.</i> , Stimulation of a low Km GTPase by inhibitors of adipocyte adenylate cyclase. <i>Molecular Pharmacology</i> (1982), 21(2), 336-42 | |

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Sheet 6 of 6

Complete if Known

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| Application Number | 10/530,902 |
| Filing Date | April 8, 2005 |
| First Named Inventor | Graeme Semple |
| Art Unit | 1626 |
| Examiner Name | Anderson, Rebecca L |
| Attorney Docket Number | 29.US2.PCT |

NON PATENT LITERATURE DOCUMENTS

| Examiner Initials * | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | T ² |
|---------------------|-----------------------|---|----------------|
| | IH | AKTORIES <i>et al.</i> , In vivo and in vitro desensitization of nicotinic acid-induced adipocyte adenylate cyclase inhibition. <i>Naunyn-Schmiedeberg's Archives of Pharmacology</i> (1982), 318(3), 241-5 | |
| | II | FRANCESCHI <i>et al.</i> , Synthesis and aggregation of two-headed surfactants bearing amino acid moieties. <i>New Journal of Chemistry</i> (1999), 23(4), 447-452 | |
| | IJ | OGAWA <i>et al.</i> , Identification of metabolites of the acaricide, tebufenpyrad, formed in in vivo and in vitro systems of rats. <i>Nippon Noyaku Gakkaishi</i> (1994), 19(3), 169-79 | |
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| | IL | CABILDO <i>et al.</i> , Carbon-13 NMR chemical shifts of N-unsubstituted and N-methylpyrazole derivatives. <i>Organic Magnetic Resonance</i> (1984), 22(9), 603-7 | |
| | IM | SAHA <i>et al.</i> , Design, synthesis and spectroscopic characterization of palladium(II) and platinum(II) complexes of pyrazole-derived ligands with potential anti-tumor properties in its historical perspective. <i>Polyhedron</i> (1994), 13(13), 2025-33 | |
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| | IO | BARALDI <i>et al.</i> , An efficient procedure for the synthesis of 5H-6-substituted pyrazolo[1,5-d]-1,2,4-triazine-4,7-diones. <i>Synthesis</i> (1999), (3), 453-458 | |
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| | IR | OFFERMANN, The nicotinic acid receptor GPR109A (HM74A or PUMA-G) as a new therapeutic target. <i>Trends in Pharmacological Sciences</i> (2006), 27(7), 384-390 | |
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| | IT | HOLLAND <i>et al.</i> , Heterocyclic tetrazoles, a new class of lipolysis inhibitors. <i>Journal of Medicinal Chemistry</i> (1967), 10(2), 149-54 | |

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| Examiner Signature | Date Considered |
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